OPEN PEER REVIEW REPORT 1

Name of journal: Neural Regeneration Research
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Title: The role of lysosomes in the etiology of Parkinson's disease
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Reviewer's country: USA

COMMENTS TO AUTHORS

In this manuscript, the author very briefly touched on how the ALP function and autophagy may be linked with the pathogenesis of PD and discussed about when impairment of ALP function starts to contribute to the pathological progression. In general, the manuscript failed to summarize the current literature and provide a comprehensive discussion about of the role of lysosomes in PD. My specific comments are as follow.

1. The structure of the manuscript is not of publish quality. The logic flow is unclear.

2. The authors never made a comprehensive summary of the current knowledge on the role of lysosomes in PD, even though the title is named "The role of lysosomes in the etiology of Parkinson's disease".

First, the authors only touched on the ALP pathway, while other lysosomal genes and lysosomal related pathways, including the endo-lysosomal trafficking and retromer function pathway, have been also suggested to be closed link to PD. For example, TMEM175, which encodes a H+ channel on the lysosome membrane, is a high-risk factor of PD in GWAS, and VPS35, a gene encoding the core component of the retromer complex, is the cause of late-onset familial Parkinson's disease. Can the author discuss about the genes functioning in the different lysosome-related pathways and how they might be contributing to the pathogenesis of PD based on current literature?

Second, while the author mainly focused on the ALP pathway, still, no in-detail discussion was made about how autophagy is defected in PD patients and how that may contribute to the pathogenesis and progression of the disease. For example, what are the evidence in literature that may suggest neuronal dysfunction and proteinopathy occur separately?

Third, the author mostly discussed the role of neurons in PD. Recent research has shown that glial cells, including microglia and astrocytes, have critical roles in the pathogenesis of PD. Can the author elaborate on this in the manuscript? What is the current knowledge of the role of lysosomes in glia in PD?

The current figure is insufficient to illustrate the key points of the manuscript. A figure summarizing the different lysosome-related genes and pathways in PD would be helpful.